REMARKS

By this amendment, claim 1 is amended as discussed below. Claims 1-7, 9, 12 and 15-18 are pending. Support can be found in the specification as filed, for example at page 19. No issue of new matter arises.

Rejections under 35 U.S.C. §103(a)

Claims 1-7, 9, 12 and 15-16

Claims 1-7, 9, 12 and 15-16 were rejected under 35 U.S.C. 103(a) as allegedly "being unpatentable over Seemann (Canadian Patent Application 2,062,047; laid open to the public on 8/29/1992, of record) in view of Mattes (U.S. Patent 4,859,449; issued 08/1989, of record) or Winkelhake (Winkelhake,J. Biological Chemistry, 251 (4): 1074-1080, 1976, of record) or Day et al .Oournal of Biological Chemistry 1980; 255: 2360-2365)."

Seemann is alleged to teach "a fusion protein comprising the general formula huTuMAb-L-β-gluc, wherein huTuMA is a humanized tumor-specific moloclonal antibody or fragment thereof, L is a linker and β-gluc comprises human β-glucuronidase (page 1, 1st paragraph)." Seemann is also alleged to teach "that the huTuMAb includes the antibody binding fragments of antiCEA BW431/26 monoclonal antibody (page 3, lines 16-23; page 17, lines 25+; and page 23, *Example* 0)." Finally, Seemann is alleged to teach that "fusion proteins can be further modified in order to achieve an increased half-life, wherein the fusion proteins are treated with an oxidizing agent which cleaves the carbohydrate ring, e.g. chemical degradation, which can be further derivatized by reductive animation which generates a new carbohydrate residue (page 4, lines 12-30)" and "a pharmaceutical composition comprising the fusion protein".

The Office Action then acknowledges that "Seemann does not explicitly teach that the fusion proteins or conjugates comprise an exposed galactose, mannose, N -acetylglucosamine, lactose, N -acetyllactose, glucose or fucose."

To remedy the acknowledged deficiencies of Seemann the Office Action proposes "to modify the fusion protein taught by Seemann with a mannose, as well as galactose or glucose in view of the teachings of Mattes, Winkelhake or Day et al because both Mattes and Day teach the

increased clearance of modified antibodies is via the Ashwell receptors (asialoglycoprotein receptors) in the liver that recognize sugars such as galactose or mannose."

Applicants amend claim 1 as shown above to recite "and wherein the amount of the carbohydrates given as mol monosaccharide/mol fusion protein is 7.04 of mannose, 4.35 of N-acetyl glucosamine, 0.6 of fucose and 0.54 of N-acetylneuraminic acid," and respectfully traverse this rejection.

The disclosure at page 19 as reproduced below clearly shows unexpected results. Accordingly, even if a *prima facie* case of obviousness has been established by the Office, such case is "rebuttable by evidence of superior or unexpected results". See, e.g., the MPEP at 716.02(a) and 2144.09.

> "FUP that has been expressed in CHO cells is removed from the plasma appreciably more efficiently than the fusion protein expressed in BHK cells, so that tumor.: plasma ratios of > 15 are reached by day 3 in the case of the CHO fusion protein. In the case of the BHK fusion protein, the corresponding ratios are < 1 (Table 8). On day 7, the tumor:plasma ratios for the CHO fusion protein are in the region of 130 while those for the BHK fusion protein are in the region of 20 (Table 8).
>
> These highly significant pharmacokinetic differences between the humanized two-chain fusion protein expressed in CHO cells or expressed in BHR cells can be explained by differences in the carbohydrate content of the fusion proteins. An analysis of the monosaccharide components in the carbohydrate content of the fusion protein expressed in BHR or CHO cells is given in Table la. Differences are observed mainly in the content of galactose, mannose and N-acetylneuraminic acid."

The applied references do not teach or suggest the present claims, especially considering the unexpected results described in the application as filed. Thus the present claims clearly are patentable over the applied references. Reconsideration and withdrawal of this rejection are respectfully requested.

Claims 17 and 18

Claim 17 was rejected under 35 U.S.C. 103(a) as being allegedly "unpatentable over Seemann (Canadian Patent Application 2,062,047; laid open to the public on 8/29/1992, of record) in view of Mattes (U.S. Patent 4,859,449; issued 08/1989, of record) or Winkelhake (Winkelhake, J. Biological Chemistry, 251(4): 1074-1080, 1976, of record) or Day et al. (Journal of Biological Chemistry 1980 and further in view of Bosslet (Bosslet et al, Br. J. Cancer 65: 234-238, 1992) and Jahde (Jahde et al, Cancer Res. 52: 6209, 1992;)."

And Claim 18 was rejected under 35 U.S.C. 103(a) as being allegedly "unpatentable over Seemann (Canadian Patent Application 2,062,047; laid open to the public on 8/29/1992, of record) in view of Mattes (U.S. Patent 4,859,449; issued 08/1989, of record) or Winkelhake (Winkelhake, J. Biological Chemistry, 251(4): 1074-1080, 1976, of record) or Day et al.(Journal of Biological Chemistry 1980) and further in view of Bagshawe (U.S. Patent 5,632,990; issued 05/1997; filed 12/1990)."

The additional applied references merely were cited to mention additional elements recited in these claims. Claims 17 and 18 depend from claim 1 and therefore are patentable over applied art for at least the same reasons that claim 1 (and claim 16) is patentable over the applied art.

Reconsideration and withdrawal of these rejections are respectfully requested.

Conclusion

Entry of the amendment is proper under 37 C.F.R. §1.116 because the amendments a) place the application in condition for allowance; b) do not raise new issues requiring further search and/or consideration; c) place the application in better condition for appeal should an appeal be necessary.

In view of the above amendments and remarks, Applicants respectfully request reconsideration and withdrawal of all rejections. Applicants respectfully submit that the application is now in condition for allowance and request prompt issuance of a Notice of Allowance. Should the Examiner believe that anything further is desirable that might put the application in even better condition for allowance, the Examiner is requested to contact the undersigned at the telephone number listed below.

Fees

No fees not otherwise provided for are believed to be necessitated by the instant response. However, should this be in error, authorization is hereby given to charge Deposit Account no. 18-1982 for any underpayment, or to credit any overpayments.

Respectfully submitted,

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